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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/759,837	01/16/2004	Henry Fliss	13595ZYX	8738

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SCULLY SCOTT MURPHY & PRESSER, PC
400 GARDEN CITY PLAZA
SUITE 300
GARDEN CITY, NY 11530

EXAMINER	
HENLEY III, RAYMOND J	

ART UNIT	PAPER NUMBER
1614	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/759,837	FLISS, HENRY	
	Examiner	Art Unit	
	Raymond J. Henley III	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 January 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *19 and 46-59* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *19 and 46-59* is/are rejected.

7)☒ Claim(s) *47-49,51 and 54* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *January 16, 2004*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

CLAIMS 19 AND 46-59 ARE PRESENTED FOR EXAMINATION

The Preliminary Amendment and Information Disclosure Statement filed January 16, 2004 have been received and entered into the application. Accordingly, the specification at page 1 has been amended; claims 1-18 and 20-45 have been canceled; and claims 46-59 have been added. Also, as reflected by the attached, completed copies of form PTO-1449, (3 sheets), the cited references have been considered.

Specification

The specification at page 1, as amended, is objected to under 37 C.F.R. § 1.78(a) and MPEP § 201.11 as being incomplete in not setting forth the current status of Serial No. 10/205,973 as U.S. Patent No. 6,889,774. Appropriate correction is required.

Also, Office records indicate that applicants are entitled to claim benefit to Provisional Application Serial No. 60/140,632, filed June 23, 1999. This application, however, does not appear in the amendment to page 1 of the specification. Applicant is requested to either (i) further amend the specification at page 1 to indicate that benefit is sought or (ii) provide a statement that such benefit is not sought.

For the purposes of examination the effective date of the present application will be that of the earliest parent application listed on page 1 of the specification, i.e., Serial No. 09/602,829, filed June 23, 2000, now U.S. Patent No. 6,407,090.

Claim Objections

Claim 54 is objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim must refer to other claims in the alternative. See MPEP § 608.01(n).

Thus, in order to overcome the present objection, claim 54 should be amended at line 1 such that "19 and 46-53" reads as ---19 or 46-53---.

Claims 47-49 and 51 are objected to as failing to further limit the subject matter of the claim from they depend. In particular, claims 47 and 51 define a step of administration. However, because the claims from which they depend define compositions, and because compositions are static, a step of administration fails to impart any further feature(s) to the previously defined composition.

Claim Rejection - 35 USC § 112, First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 50-54 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a pharmaceutical composition effective for treating or inhibiting ischemia, does not reasonably provide enablement for such composition effective for preventing ischemia. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The present specification is evaluated by the Examiner as directed by the Court in *In re Marzocchi et al.* , 169 USPQ 367 (CCPA 1971):

"Specification disclosure which contains teaching of manner and process of making and using the invention in terms corresponding to the scope to those used in describing and defining subject matter sought to be patented must be taken as in compliance with enabling requirement of first paragraph of 35 U.S.C. 112 *unless there is reason to doubt the objective truth of statements contain therein which must be relied on for enabling support*; assuming that sufficient reason for such doubt exists, a rejection for failure to teach how to make and/or use will be

proper on that basis, such a rejection can be overcome by suitable proofs indicating that teaching contained in specification is truly enabling." (emphasis added).

Here, the objective truth of the statement that ischemia may be prevented is doubted in light of applicants' specification at page 10 where, at best, it is indicated that neuro*protection* may be provided rather than the more rigorous objective of prevention. In particular, it is disclosed at lines 21-29 that "For example, zinc pyrithione demonstrates neuroprotective properties, showing protection against cell loss in the selectively vulnerable zone of the CA1 region of the hippocampus in a rat model of severe global ischemia. In the mouse model of severe focal ischemia, zinc pyrithione demonstrates neuroprotective properties, significantly decreasing brain infarct volume and neurological deficit.

Further, nothing in the examples in the present specification show anything that provide a reasonable basis for concluding that ischemia may be prevented.

Here, as per MPEP § 2111, the term "preventing" is taken to be synonymous with the term "curing" and both circumscribe methods of treatment having absolute success. Because absolute success is not reasonably possible with most diseases/disorders, especially those having etiologies and pathophysiological manifestations as complex or not fully understood as ischemia, in general, the specification is deemed as lacking an adequate enabling disclosure of the same such that the skilled artisan would not be able to do what applicant is claiming with at least a reasonable expectation of success.

It is suggested that claim 50 be amended to recite, in-part, "A pharmaceutical composition effective in treating or ~~preventing~~ inhibiting ischemia..." in order to overcome this rejection.

Claim Rejection - 35 USC § 112, Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 48, 49, 52, 53 and 56-59 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claims are considered indefinite because in defining the amount of active agent contained in the composition, reference is not made to an element of the composition, e.g., volume, but rather is made to an element that is not a part of the claimed composition, i.e., kg of body weight, and which is variable depending on the particular body. See MPEP § 2173.05(b) under the heading "Reference to an Object That is Variable May Render a Claim Indefinite".

This rejection may be overcome by amending the claim to indicate the amount of the zinc ionophore as a concentration, such as is disclosed in the present specification at page 9, lines 7-8, i.e., about 600 pM to about 15 μM.

Claim Rejection - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

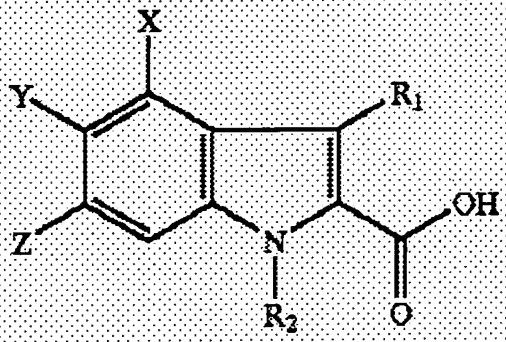
Claims 19, 46, 47, 50, 51, 54 and 55 are rejected under 35 U.S.C. 102(a) as being anticipated by Bernard et al., (FR 2,768,146; March 12, 1999; "Bernard '146") as evidenced by Bernard et al., (U.S. Patent No. 6,448,285; Bernard '285).

For the purposes of examination, an English translation of Bernard '146 will be relied upon as the basis for the present rejection. The English translation is Bernard '285. Both Bernard '146 and '285 are derived from the same PCT publication; (i.e., WO 99/12905 A1; see the Derwent abstract page cited on the attached form PTO-892 showing that the PCT publication, Bernard '146 and Bernard '285 belong to the same patent family) and in light of such a fact, the '285 patent is reasonably expected to contain the same subject matter as the '146 document. The Examiner relies on the MPEP at §901.05, which states, "It is possible to cite a foreign language specification as a reference, while at the same time citing an English language version of the specification with a later date as a convenient translation if the latter is in fact a translation."

The present claims define compositions comprising a zinc ionophore, such as zinc pyrithione, heterocyclic amines, dithiocarbamates and vitamins, (claim 54), in amounts which, for an average 70 kg human male, range from either 0.35 μg – 350 mg, (e.g., claim 48), or 14 μg to 42 mg, (e.g., claim 49). The compositions may further contain a pharmaceutically acceptable carrier, (e.g., claim 19), and be presented in forms such as an injectable preparation, (claim 55), or a tablet, (claim 56). The claims further include recitations of intended use, e.g., "effective in protecting tissue against apoptosis *in vivo*", (claim 19). Because the recitations do not impart any physical or otherwise material feature to the compositions, such are not provided any patentable significance in defining over compositions disclosed in the prior art otherwise meeting the physical requirements of the present claims.

Bernard '285 teaches a pharmaceutical composition comprising a heterocyclic amine compound, (a.k.a., a zinc ionophore, see present claim 54), of the formula:

Formula (I)



in which X and Y, which may be identical or different,

represent a hydrogen atom or a radical —O—CHR_3R_4, in which R_3 is a hydrogen atom or an optionally substituted phenyl radical or alternatively a 5- or 6-membered heterocycle and R_4 is an optionally substituted phenyl radical or alternatively a 5- or 6-membered heterocycle, or R_3 and R_4 taken together form, with the carbon atom, a 5- or 6-membered ring or heterocycle;

or, taken together, form, with the 2 carbon atoms bearing them, a ring or a heterocycle containing 5 or 6 carbon atoms;

Z represents a hydrogen atom or a radical —O—R_5 in which R_5 is a C_1–C_6 alkyl radical or a C_6–C_{12} aralkyl radical;

R_1 represents a hydrogen atom or a C_1–C_6 alkyl radical or a C_6–C_{12} aralkyl radical which is optionally substituted;

R_2 represents a hydrogen atom or a C_1–C_6 alkyl radical or a radical —CHR_3R_4, in which R_3 and R_4 have the above definitions;

and a pharmaceutically acceptable carrier, where the composition may be in the form of an injectable preparation or a tablet and the heterocyclic amine is present in concentrations ranging

from 0.001% to 5% by weight (see col. 3, lines 57-61; col. 6, lines 55-58; and cols. 26-27, claims 1-12).

Claim Rejection - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 19 and 46-59 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bernard '285, for the reasons set forth *supra* which reasons are here incorporated by reference.

The difference between the above and the claimed subject matter lies in that Bernard '285 fails to disclose a composition comprising other compounds defined by applicant as a zinc ionophore with sufficient specificity so as to place the claimed subject matter in the possession of the public as well as the presently claimed dosage amounts thereof.

However, the difference between the subject matter sought to be patented and the prior art is such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains because Bernard '285 further discloses compounds which meet the present definition for a zinc ionophore as active agents which may be used in combination with the disclosed heterocyclic amine compound. In particular, Bernard '285 teaches that compounds including vitamin A, vitamin E, (col. 7, line 56), benzyl nicotinate, (a.k.a., another heterocyclic amine compound, col. 8, line 1), vitamin D, (col. 8, line 11), and zinc pyrithione, (col. 8, line 45). In the present claims, the dosage amounts may vary according to the weight of an unknown body and thus would

appear to not be inconsistent with the variable concentrations specifically disclosed by Bernard '285, i.e., from 0.001% to 5% by weight (see col. 3, lines 57-61).

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 19 and 46-59 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over (i) claims 1-26 of U.S. Patent No. 6,407,090, (cited by applicant), (ii) claims 1-26 of U.S. Patent No. 6,495,538, (cited by applicant) or (iii) U.S. Patent No. 6,689,774, (cited by the examiner). Although the conflicting claims are not identical, they are not patentably distinct from each other because the presently claimed compositions are necessary for the practice of the methods of the above cited patents. Because the presently claimed compositions would be in possession of those practicing the claimed methods, no patentable distinction can be seen between the compositions employed in the patented claims and that of the present claims.

None of the claims are currently in condition for allowance.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Raymond J. Henley III whose telephone number is 571-272-0575. The examiner can normally be reached on M-F, 8:30 am to 4:00 pm Eastern Time.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin H. Marschel can be reached on 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Raymond J. Henley III
Primary Examiner
Art Unit 1614

November 29, 2006